

REMARKS

Claim 1 has been amended to recite that the surfactant mixture has a hydrophilic-lipophilic balance (HLB) of from 3 to 5. Support for the claim can be found in claim 3 as originally recited. Claim 12 has been amended to correct a typographical error.

Claims 23, 24, and 25 have been added. Support for these claims can be found at line 28 on page 12 of the specification and claims 3 and 14 as originally recited.

Claim 3 has been canceled herein without prejudice on the merits, its subject matter having been incorporated into claim 1.

Claims 2, 7, 9, and 18-19 were previously canceled.

Claims 1, 4-6, 8, 10-17, and 20-25 are pending and under consideration.

Rejection of Claims 1, 3-6, 8, 10-13, 15, and 20 under 35 U.S.C. §103(a) over Kim et al. ("Kim") (*Journal of Microencapsulation*, 2002 19(6):811-22) in View of Hassan (U.S. Patent Publication 2002/119916)

Applicants maintain that it would not be obvious to a practitioner in the art that a surfactant allegedly suitable for separating a water phase from an oil phase (*i.e.* sorbitan sesquioleate), as taught by Hassan, is also suitable for separating a first oil phase from a second oil phase (*i.e.*, Span 80), as taught by Kim. The Office has cited Kim's teachings regarding acetonitrile being polar, water-miscible, and oil-immiscible as indicating that acetonitrile could be separated from oil with a surfactant used to separate water from oil. This is traversed on the ground that Kim does not use acetonitrile in a manner that resembles the properties of water, *i.e.*, as a water-miscible and polar solvent. Kim explicitly teaches:

With oil as a processing medium, use of acetonitrile alone as a dispersed medium did not ensure formation of a stable emulsion, and a non-polar solvent such as dichloromethane was included to decrease polarity of the acetonitrile solution. In this study, the mixed solvent system comprising 1:1 proportions of acetonitrile and dichloromethane was used. (Kim at first full paragraph on page 815)

Applicants therefore maintain that it is not obvious that any particular surfactant taught for use in the water-in-oil or oil-in water emulsions of Hassan would work in the oil-in-oil emulsion system of Kim. In view of the foregoing as well as the fact that Kim and Hassan do not teach

overlapping species of surfactants, it is not obvious to substitute the Span 80 taught by Kim with the sorbitan sesquioleate taught by Hassan.

Applicants further submit that the specification shows unexpected results commensurate in scope with the claimed invention as now recited. The specification shows that mixtures of at least two surfactants having combined HLBs within the range of 3-7, which includes the recited range of 3-5, unexpectedly produce microparticles with suitable morphology.

As shown in Examples 3 and 4 of the specification (pages 12-13), various mixtures of surfactants at a combined HLB of about 3.7 produced spherical non-aggregated, non-porous particles in the required size range. These mixtures included sorbitan sesquioleate (Arlacel 83), which is an equimolar mixture of sorbitan monoleate and sorbitan dioleate; a mixture of 14.4% Tween 80 and 85.6% Span 85; and a mixture of 56.5% Span 80 and 43.5% Span 85. As shown in Example 16 of the specification (page 18), mixtures of surfactants with combined HLBs ranging from 3-7 also produced microparticles with acceptable morphology. These mixtures included a mixture of 50% Span 80 and 50% Span 85 (HLB 3); a mixture of 53% Span 85 and 47% Span 20 (HLB 5); a mixture of 60% Span 80 and 40% Span 20 (HLB 6); and a mixture of 35% Span 80 and 65% Span 20 (HLB 7).

In contrast to such mixtures, single surfactants within the same HLB range failed to produce microparticles with acceptable morphology. Span 80 alone, which has an HLB of 4; Brij 52 alone, which has an HLB of 5.3; and Brij 92 alone, which has an HLB of 4.9, each failed to produce microparticles with acceptable morphology (see Example 1 at page 12, lines 16-23 of the specification and Example 2 on pages 11-12 of specification). It is notable that Span 80 can have vastly different effects depending on whether it is mixed with at least a second surfactant within the recited HLB range, as described above.

In view of the foregoing, pending claims 1, 4-6, 8, 10-13, 15, and 20 are not obvious over Kim and Hassan because the unique ability to form suitable microparticles with a mixture of at least two surfactants having a combined HLB of from 3 to 5 is unexpected.

The Office has alleged that Haw ("The HLB System," Uniqema, 9 March 2004, 39 pages) teaches "surfactants with HLB values of 1-3 are useful for oil/oil emulsions" (Office Action dated December 14, 2011 at second full paragraph on page 10). Haw, however, is silent regarding the unique properties of a mixture of at least two surfactants having a combined HLB

of from 3 to 5. Therefore, the subject matter of pending claims 1, 4-6, 8, 10-13, 15, and 20 is unexpected over Haw.

The Office has alleged that the solvent system appears to be crucial to the success of the surfactant system and that the claims are not commensurate in scope with Applicant's showing of unexpected results because the claims do not limit the solvent system (Office Action dated December 14, 2011 at paragraph spanning pages 10 and 11). This is traversed. The Office has based the allegation that the solvent is crucial to the success of the surfactant system only on the on the failure of Span 65 to dissolve in liquid paraffin or in an acetone/methanol mixture. However, Span 65 is a single surfactant with an HLB of less than 2 and therefore does not fall within the scope of the claims. By contrast, various solvents were tested in Example 6 of the specification (pages 14-15) with a surfactant falling within the scope of the claims, sorbitan sesquioleate. The conclusion from this experiment states:

The choice of solvent has little effect on the morphology of the microparticles. This provides evidence that the choice of surfactant is more crucial than the choice of polymer solvent. (specification at first full paragraph on page 15)

The Office has failed to provide any evidence that the solvent is crucial to the success of the system falling within the scope of the claims. Applicants therefore maintain that the showing of unexpected results is commensurate with the scope of the claims.

In view of the foregoing, Applicants submit that claims 1, 4-6, 8, 10-13, 15, and 20 are not obvious over Kim and Hassan. Withdrawal of this rejection is requested.

Rejection of Claim 16 under 35 U.S.C. §103(a) over Kim in View of Hassan and Further in View of Satturwar et al. ("Satturwar") (*International Journal of Pharmaceutics*, Vol. 218, 2001, pages 1-11)

This rejection is traversed for the reasons expressed above with respect to the rejection over Claims 1, 3-6, 8, 10-13, 15, and 20 over Kim and Hassan. The teachings of Satturwar do not address the shortcomings of Kim and Hassan. Withdrawal of this rejection is requested.

Rejection of Claims 1, 3, 4, 10, 14, 17, 21, and 22 under 35 U.S.C. §103(a) over Burnside et al. (“Burnside”) (U.S. Patent 5,824,638) in View of Pather et al. (“Pather”) (U.S. Pat. Pub. 2003/0077306)

This rejection is traversed on the ground that Burnside in view of Pather does not teach a method of producing microparticles that comprises a step of evaporating the solvent.

Burnside and Pather merely teach generating emulsions. They do not teach a method of producing microparticles that comprises a step of evaporating the solvent. See abstract of each of Burnside and Pather.

Further, it would not be obvious to modify Burnside to include a step of evaporating the solvent. Burnside require that the solvent not be dissolved, as the solvent’s continued presence in the emulsion is required to protect the drug (insulin) from proteolytic enzymes in digestive fluids. See Burnside at column 4, lines 1-11. A proposed modification cannot render the prior art unsatisfactory for its intended purpose or change its principle of operation. See MPEP §§2143.01(V) and 2143.01(VI); *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984); and *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

Claims 1, 4, 10, 14, 17, 21, and 22 are therefore not obvious over Burnside in view of Pather. Withdrawal of this rejection is requested.

New Claims

New Claims 23, 24, and 25 each ultimately depend from claim 1 and are patentable at least for the reasons expressed above for claim 1.

CONCLUSION

Applicant submits the application is now in condition for allowance. The Commissioner is authorized to charge any fees or credit any overpayments relating to this application to deposit account number 18-2055.

For the Applicant,

A handwritten signature in black ink, appearing to read 'Daniel A. Blasiolo', written over a horizontal line.

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